DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

0266 '00 FEB 18 P3:24

FEB 17 2000

Lachman Consultant Services, Inc.
Attention: Robert W. Pollock
1600 Stewart Avenue
Westbury, NY 11590

Docket No. 99P-1267/CP1

Dear Mr. Pollock:

This is in response to your petition filed on May 6, 1999, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Clozapine Tablets 12.5 mg. The listed drug product to which you refer in your petition is Clozaril® (Clozapine) Tablets, 25 mg, manufactured by Novartis Pharmaceuticals Corp. We have reviewed your petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act) and have determined that it is approved. This letter represents the Agency's determination that an ANDA may be submitted for the above-referenced drug product.

Your request involves a change in strength from that of the listed drug product (i.e., from 25 mg to 12.5 mg) . The change you request is the type of change that is authorized under the Act.

Under Section 505(j)(2)(C)(i) of the Act, the Agency must approve a petition seeking a strength, which differs from the strength of the listed drug product unless it finds that investigations must be conducted to show the safety and effectiveness of the strength.

The Agency finds that the change in strength does not pose questions of safety or effectiveness because the uses and route of administration of the proposed drug product are the same as that of the listed drug product. In addition, the 12.5 mg dose of Clozapine is recommended in the approved labeling. The approved labeling states, "It is recommended that treatment with Clozaril® (clozapine) begin with one-half of a 25 mg tablet (12.5 mg) once or twice daily and then be continued with daily dosage increments of 25-50 mg /day, if well tolerated, to achieve a target dose of 300-450 mg/day by the end of two weeks." The Agency concludes, therefore, that investigations are not necessary in this instance. In addition, if shown to meet bioavailability requirements, the proposed drug product can be expected to have the same therapeutic effect as the listed reference drug product.

The approval of this petition to allow an ANDA to be submitted for the above-referenced drug product does not mean that the Agency has determined that an ANDA will be approved for the drug product. The determination of whether an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the Agency.

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To permit review of your ANDA submission, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug product will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you submit your protocol to the Office of Generic Drugs, Division of Bioequivalence for this drug product prior to the submission of your ANDA. The Agency has published the Guidance Clozapine Tablets in Vivo Bioequivalence and in Vitro Dissolution Testing on the FDA's internet site: http://www.fda.gov/cder/guidance/index.htm, which may aid you in the design of your protocol. During the review of your application, the Agency may require the submission of additional information.

The listed drug product to which you refer in your ANDA must be the one upon which you based this petition. In addition, you should refer in your ANDA to the appropriate petition docket number cited above, and include a copy of this letter in the ANDA submission.

A copy of this letter approving your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research